REMARKS

Amendments to the specification

Applicant has amended the first paragraph of the instant application to perfect the priority claims. Specifically, Applicant has deleted the priority claims to U.S. Patent Application No. 10/427,160 and those in its priority chain (whether or not listed previously), and thereby expressly disclaims this claim of priority.

The Amendments

Claims 1, 3, 16, 21, and 33 have been amended. Claims 13-15, 18-20, 32, and 34 have been canceled herein without prejudice or disclaimer. New claims 35-65 have been added. Accordingly, claims 1, 3, 16-17, 21, 30-31, 33, and 35-65 are pending in this application.

Specifically, claim 1 has been amended to correct a typographic error in part (a), and to remove certain redundant language in parts (c) and (d). Claim 1 has been further amended in part (e) to recite "50 percent or more of the nucleotides in each strand comprise a 2'-sugar modification, wherein the 2'-sugar modification of any of the pyrimidine nucleotides differs from the 2'-sugar modification of any of the purine nucleotides." Claims 3, 16 and 33 have been amended to remove redundancies without affecting the scope of these claims. Claim 21 has been amended to depend from new claim 47.

All pending claims are fully supported not only by the as-filed application but also by the priority applications, for example, PCT/US03/05028 and U.S. Provisional Application No. 60/363,124. To facilitate substantive examination, Applicant submits below a table listing representative but non-exhaustive examples of support found in the instant application as well as in those two priority applications.

Claim #	Support in as-filed application	Support in PCT/US03/05028	Support in 60/363,124
1	p.8, ll. 5-7; p. 9, ll. 21-22; p.10, ll. 10-15; p.10, l. 27-p. 11, l. 21; p. 12, ll. 23-27; p. 13, ll. 6-17, 27-31; p. 15,	p. 7, ll. 1-7; p. 10, ll. 12-20; p. 11, ll. 12-20; p. 12, ll. 22-28; p. 14, l. 29-p. 15, l. 14; p. 24, ll.	p. 5, ll. 13-17; p. 9, l. 14-p. 10, l. 16; p. 11, ll. 12-25; p. 12, ll. 4-12; p. 15, ll. 6-9; p.

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	ll. 13-17; p. 17, ll. 7-17; p. 20, ll. 12-21; p. 21, ll. 5-9; p. 22, ll. 12-15; p. 24, ll. 10-29; p. 34, ll. 7-12; Tables III & IV	5-10; Tables IV & V	26, ll. 3-9; Tables I & III
3	p. 16, ll. 7-8	p. 8, ll. 27-28	p. 15, ll. 3-6
16	p. 17, ll. 21-27; p. 23, ll. 1-4	p. 10, ll. 21-27; p. 27, ll. 15-19; p. 30, ll. 13-15	p. 10, ll. 3-11; p. 11, ll. 11-25
17	p. 17, ll. 27-28; p. 38, ll. 1-13	p. 26, ll. 5-16	p. 13, l. 18-p. 14, l. 9
21	p. 19, ll. 11-13; p. 23, ll. 4-6	p. 11, ll. 8-10; p. 15, ll. 15-16	p. 9, ll. 21-25; p. 22, ll. 12-25, 30-31;
30	p. 20, ll. 10-11; p. 30, ll. 16-19	p. 11, ll. 28-29; p. 20, ll. 8-12	p. 18, ll. 15-19
31	p. 24, ll. 30-31	p. 46, ll. 19-21	p. 9, ll. 5-7
33	p. 12, ll. 16-20	p. 11, ll. 12-20	p. 13, ll. 3-7
35	p. 12, ll. 23-27, p. 20, ll. 12-30; p. 31, l. 16-p. 32, l. 20	p. 21, ll. 23-28; Table IV	p. 5, ll. 14-17; p. 9, l. 14-p. 10, l. 16; p. 11, ll. 12-15
36	p. 20, ll. 2-4; p. 31, l. 28-p. 32, l. 2; Tables III & IV	p. 23, ll. 16-21; Table IV	p. 10, ll. 11-16, 25-30; p. 11, ll. 6-11, 20-25
37	p. 17, ll. 7-10; Tables III & IV	p. 23, ll. 16-21; Table IV	p. 10, ll. 11-16, 25-30; p. 11, ll. 6-11, 20-25
38	p. 17, ll. 7-17; p. 18, ll. 1-3; p. 22, ll. 21-28; p. 40, ll. 1-29; p. 41, ll. 10-19; p. 41, l. 30-p. 42, l. 7; Tables III & IV	p. 23, ll. 16-21; p. 28, ll. 4-12; p. 28, l. 24-p. 29, l.4; p. 29, ll. 16-24; Table IV	p. 10, ll. 11-16, 25-30; p. 11, ll. 6-11, 20-25
39	p. 17, ll. 7-17; p. 22, ll. 21-25; p. 40, ll. 1-29; Tables III & IV	p. 23, ll. 16-21; p. 28, ll. 4-12; Table IV	p. 10, ll. 11-16, 25-30; p. 11, ll. 6-11, 20-25
40	p. 17, ll. 7-17; p. 22, ll. 22-28; p. 41, ll. 10-19; p. 41, l. 30-p. 42, l. 7; Tables III & IV	p. 23, ll. 16-21; p. 28, l. 24-p. 29, l. 4; p. 29, ll. 16-24; Table IV	p. 10, ll. 11-16, 25-30; p. 11, ll. 6-11, 20-25
41	p. 17, ll. 7-17; Tables III & IV	p. 23, ll. 16-21; Table IV	p. 10, ll. 11-16, 25-30; p. 11, ll. 6-11, 20-25
42	p. 17, ll. 10-12, 15-17; p. 19, ll. 10-11; p. 22, ll. 23-25, 28-30; p. 40, ll. 10-29: Tables III & IV	p. 28, l. 24-p. 28, l. 4; Table IV	p. 10, ll. 3-11, 17-25, Table I

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43	p. 17, ll. 7-10, 13-15; p. 19, ll. 3-9; p. 22, ll. 21-23, 25-28; p. 40, ll. 1-20; p. 41, l. 30-p. 42, l. 7; Tables III & IV	p. 11, ll. 1-8; p. 28, ll. 4-12; p. 29, ll. 16-24; Table IV	p. 10, ll. 3-11, 17-25, Table I
44	p. 17, ll. 7-12; p. 22, 21-25; p. 40, ll. 1-29; Tables III & IV	p. 11, ll. 1-8; p. 28, ll. 4-12; Table IV	p. 10, ll. 3-11, 17-25, Table I
45	p. 17, ll. 15-17; p. 19, ll. 3-11; p. 25, ll. 25-30; Tables III & IV	p. 28, l. 24-p. 29, l. 4; p. 29, ll. 16-24; Table IV	p. 10, ll. 3-11, 17-25, Table I
46	p. 17, ll. 15-17; Tables III & IV	Table IV	p. 10, ll. 3-11, 17-25, Table I
47	p. 18, ll. 12-13; p. 19, ll. 11-13; p. 26, ll. 21-27; Tables III & IV	p. 11, ll. 16-18; p. 23, ll. 22-24	p. 9, ll. 16-19; p. 11, l. 26-28; Table I
48	p. 42, l. 17-p. 43, l. 2; Tables III & IV	p. 30, l. 20-p. 31, l. 3; Tables IV & V	p. 5, ll. 13-17; p. 9, l. 14-p. 10, l. 16; p. 11, ll. 12-25; p. 12, ll. 4-12; p. 15, ll. 6-9; p. 26, ll. 3-9; Tables I & III
49	p. 43, ll. 9-10; p. 43, ll. 23-32; Tables III & IV	p. 21, ll. 23-28; Table IV	p. 5, ll. 14-17; p. 9, l. 14-p. 10, l. 16; p. 11, ll. 12-15
50-54	p. 42, l. 17-p. 43, l. 2; Tables III & IV	p. 12, ll. 16-21; p. 28, ll. 4-12; Table IV	p.10, ll. 11-16, 25-30; p. 11, ll. 6-11, 20-25
55-56	p. 42, l. 17-p. 43, l. 2; Tables III & IV	p. 11, ll. 1-8; p. 28, ll. 4-12; Table IV	p. 10, ll. 3-11, 17-25; Table I
57	p. 43, ll. 11-17; Tables III & IV	p. 28, l. 24-p. 29, l. 4; p. 29, ll. 16-24; Table IV	p. 10, ll. 3-11, 17-25; Table I
58	p. 16, ll. 7-8; Tables III & IV	p. 8, ll. 27-28	p. 15, ll. 3-6
59	p. 43, ll. 2-5; p. 44, ll. 17-20	p. 27, ll. 15-19; p. 30, ll. 13-15	p. 10, ll. 3-11; p. 11, ll. 11-25
60	p. 38, ll. 1-13	p. 26, ll. 5-16; p. 31, ll. 3-5	p. 13, l. 18-p. 14, l. 9
61	p. 26, ll. 21-27	p. 11, ll. 8-10; p. 23, ll. 22-24	p. 9, ll. 16-19; p. 11, l. 26-28; Table I
62	p. 19, ll. 11-13; p. 23, ll. 4-6; p. 26, ll. 21-27	p. 11, ll. 8-10; p. 15, ll. 15-16	p. 9, ll. 21-25; p. 11, ll. 12-25, 30-31
63	p. 30, ll. 16-19	p. 11, ll. 28-29; p. 20, ll. 8-12	p. 9, ll. 5-7

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64	p. 43, ll. 5-7	p. 11, ll. 12-20	p. 13, ll. 3-7
65	p. 24, ll. 30-31	p. 46, ll. 19-21	p. 18, ll. 15-19

As such, the pending claims are fully supported, *inter alia,* by this and the priority applications. Applicant respectfully requests entry of the proposed amendments and urges that the claims be accorded the earliest priority date of March 11, 2002.

Restriction Requirements

The Examiner required the election of a single modified construct from the various allegedly distinct molecules of claim 1. *See* Restriction Requirement, at page 5. Specifically, for example, the Examiner stated that "with regard to claim 1, parts e and f, nucleic acid molecules that comprise from about 50 to 100% 2'-fluoro modifications are structurally distinct from those that comprise from about 50 to 100% 2'-O-methyl modifications." *Id.* Applicant traverses.

It is respectfully noted that, according to the MPEP 806.05(j), and as cited by the Examiner, related inventions are distinct if (1) the inventions as claimed are either not capable of use together *or* have a materially different design, mode of operation, function, or effect; (2) the invention do not overlap in scope; *and* (3) the invention as claimed are not obvious variants. Thus only when all three criteria are met before related inventions can be called distinct. The Examiner appeared concerned that the claimed constructs are structurally distinct, but did not note that the inventions as claimed are fully capable of use together, as taught expressly by the instant specification:

> The nucleic acid molecules of the instant invention, individually, or in combination or in conjunction with other drugs, can be used to treat diseases or conditions discussed herein (e.g., cancers and other proliferative conditions, inflammatory diseases and conditions, and/or autoimmune diseases and conditions).

Specification, at page 80, lines 12-15. The claimed constructs also do not have materially different designs, because they most definitely share common structural features, such as, for example, being double-stranded, each strand being 18-27 nucleotides in length, with the antisense strand having complementarity to a human ICAM RNA sequence, and with 50% or more of the nucleotides being chemically

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modified. They further do not have materially different biological effects because they all function by inhibiting the expression of human ICAM. Therefore, the claimed molecules are related and not patentably distinct.

Without acquiescing to the Examiner's contentions, however, Applicant has amended claim 1 to be clearly generic, therefore rendering this requirement moot.

The Examiner further required election of a "defined number of modified nucleotides and a defined overhang length" in claims 13-15, 18-20 and 32-34. Claims 13-15, 18-20, 32 and 34 have been canceled herein without prejudice or disclaimer, whereas claim 33 has been amended to no longer recite a defined overhang length, therefore rendering this restriction requirement moot.

The Examiner also required election of a single position for a terminal cap moiety in claim 16. Applicants hereby elect a construct wherein the sense strand includes a terminal cap moiety at both the 5' and the 3' ends for initial search and examination. Claims 1, 3, 16-17, 21, 30-31, 33, 35-65 are readable thereon. This election is however made with traverse, because the allegedly distinct molecules share at least some structural features (i.e., designs) and have common biological effects. The number of variations is only 3, therefore it would not be unduly burdensome to search and examine together. As such, Applicant respectfully urges the rejoinder of the non-elected constructs.

The new claims

Applicant believes that the newly submitted independent claim 48 is generic. Applicant further believes that the other new claims are drawn to related inventions that are not so distinct as to warrant restriction. However, in the interest of advancing substantive examination, and because the Examiner appeared to require election of a chemically modified construct having defined modification on each strand and each nucleotide type, Applicant hereby provides such a construct from which the initial search might be undertaken.

Concerning the nucleotides in the sense strand, Applicant elects a construct wherein any of the pyrimidine nucleotides are 2'-deoxy-2'-fluoro pyrimidines. New claims 35, 38-39, 41-51, and 53-65 (previously pending claims 1, 3, 16, 17, 21, 30,

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31, and 33) would read thereon. Applicant further elects a construct wherein any of the purine nucleotides in the sense strand are 2'-deoxy purines. New claims 35-41, 43-44, 46-53, 55-56, and 58-65 (previously pending claims 1, 3, 16, 17, 21, 30, 31, and 33) would read thereon.

Concerning the nucleotides in the antisense strand, Applicant elects first a construct wherein any of the pyrimidines are 2'-deoxy-2'-fluoro pyrimidines. New claims 35, 38, 40-50, and 52-65 (previously pending claims 1, 3, 16, 17, 21, 30, 31, and 33) would read thereon. Applicant further elects a construct wherein any of the purines are 2'-O-methyl purines. New claims 35-42, 45, 46-54, and 57-65 (previously pending claims 1, 3, 16, 17, 21, 30, 31, and 33) would read thereon.

Because the non-elected constructs are fully capable of being used together with the elected ones, and they share many common structural features and functional effects, as explained above, Applicant respectfully urges examination of all of the pending claims in their entirety.

Conclusion

In view of the foregoing remarks, Applicant respectfully requests early action on the merits. If the Examiner believes that a teleconference will expedite prosecution of this application, he is urged to telephone the undersigned at the number below.

Respectfully submitted,

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